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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,793	10/24/2001	Robert Johan Joseph Hageman	BO 42384	8792

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EXAMINER

KHARE, DEVESH

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 10/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/889,793

Applicant(s)

HAGEMAN ET AL.

Examiner

Devesh Khare

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18,19,21-25 and 28-34 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 18,19,21-25 and 28-34 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s) ____.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ 6) ☐ Other: _____

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The amendment received on 07/15/03 has been entered. Claims 16,17,20,26 and 27 have been cancelled. Claims 18,19,21-25,28-30 and newly added claims 31-34 are currently pending in this application. Rejections of claims 18,19,21-25,28-30 under 35 U.S.C 112, second paragraph, as set forth in the previous office action are withdrawn in view of applicants amendments of the claims.

35 U.S.C. 112, first paragraph rejection

Claims 16-30 are rejected under 35 U.S.C. 112, first paragraph, of record, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- (1) The quantity of experimentation necessary (time and expense);
- (2) The amount of direction or guidance presented;
- (3) The presence or absence of working examples of the invention;
- (4) The nature of the invention;
- (5) The state of the prior art;
- (6) The relative skill of those in the art;
- (7) The predictability or unpredictability of the art; and
- (8) The breadth of the claims.

The applicant's specification fails to provide sufficient guidance or support to enable the worker of ordinary skill in the art to practice methods for preventing serotonin- or

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melatonin-mediated disorders by the administration of an effective amount of a combination of folic acid, vitamin B6 and B12 and at least one component selected from the group consisting of riboflavin, thiamin, niacin and zinc. The specification describes the alleged prevention of serotonin- or melatonin-mediated disorders in a prophetic manner only. Such allegations are not considered to provide sufficient support for presuming or establishing methodological procedures for preventing serotonin- or melatonin-mediated disorders, particularly since there is not seen sufficient guidance and support in the specification or correlation of that which is disclosed with prior art teachings to support same.

Further, there is no enabling description of the administration of an effective amount of a combination of folic acid, vitamin B6 and B12 and atleast one component selected from the group consisting of riboflavin, thiamin, niacin and zinc for preventing serotonin- or melatonin-mediated disorders. The worker of ordinary skill in the art would not be able to practice the instantly claimed method given the limited guidance provided by the disclosure herein. The mere statements that the compounds of the instant invention are likely to be effective, or expected to be effective on the basis of limited *in vitro* test data, are insufficient to enable the worker of ordinary skill in the art to practice the invention commensurate in scope with these claims. It is well known and established that the "law requires that disclosure in an application shall inform those skilled in the art how to use appellant's alleged discovery, not how to find out how to use it for themselves." *In re Gardner et al.*, 166 USPQ 138(CCPA 1970).

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35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 16-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Serfontein (U.S. Patent 5,631,271) in view of Paul et al. (U.S. Patent 5,292,538) of record.

Claims 16-28 are drawn to method for the treating serotonin- or melatonin-mediated disorders with folic acid, vitamin B6 and B12 and at least one component selected from the groups consisting of riboflavin, thiamine, niacin and zinc, wherein folic acid is more than 44 µg, vitamin B12 more than 0.8 µg, vitamin B6 more than 50 µg and atleast 0.55 mg of niacin and/or at least 0.08 mg of riboflavin and/or at least 55 µg of thiamine, with further comprising carbohydrates, fats and proteins.

Serfontein teaches a composition comprising vitamin B6, folate and vitamin B12, for treatment and prophylaxis of metabolic disturbances in infants (see abstract). Serfontein disclosed a substance or composition for use in a method to enhance or stimulate the immune response system of human and animal by enhancing their methylation capacity (see col. 1, lines 6-12). Serfontein disclosed a pharmaceutical composition in col. 10, lines 38-62, that is essentially a combination of vitamin B6, folate and vitamin B12.

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Serfontein also suggest in col. 12, lines 1-10, the daily dosages of ingredients in an infant food formula in the ranges of vitamin B6 (0.01-5 mg), riboflavin (0.01-5 mg), folate (.001-0.5 mg) and vitamin B12 (0.01-10 μ g). Furthermore, under Example 10 in col. 31, an infant food formula is disclosed, wherein the protein (1.6%), fat (3.3%) and carbohydrate (67.0%) with vitamin and minerals containing 0.5 mg of folic acid, 0.17 mg of B12, 0.2 mg of zinc, 10 mg of calcium, 5 mg of magnesium and 1.0 mg of niacin is provided in a composition to treat premature infants. Serfontein differs from the applicant's invention that Serfontein does not provide an explicit example of a nutritional composition, comprising the tryptophan and/or melatonin and/or adenosine, however Serfontein does provide motivation to use vitamin B6, riboflavin, folate, vitamin B12 and protein, fat and carbohydrate, for treatment and prophylaxis of metabolic disturbances in infants. Use of a known member of a class of materials in a process is not patentable if other members of the class were known to be useful for that purpose, even though results are better than expected.

Paul et al. teach a method of providing sustained energy and nutrition for anabolic physiological state in a human by administering to said human a nutritional composition containing carbohydrates, lipids, protein and magnesium in the form of amino acid chelate and other vitamins and nutrients (see abstract). Paul et al. disclose a composition under Example in cols. 10 and 11, containing the said ingredients for use to support an anabolic physiological state in humans. It is noted that Paul et al. does not provide specific disclosures regarding the treatment of serotonin- or melatonin-mediated disorders.

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Therefore, one of ordinary skill in the art would have found the applicants claimed method for the treating of serotonin- or melatonin-mediated disorders with a pharmaceutical composition containing folic acid, vitamin B12, vitamin B6, and further containing at least one group consisting of riboflavin, thiamin, niacin and zinc, to have been obvious at the time the invention was made having the above cited references before him. Since Serfontein teaches a composition comprising the pyridoxal in combination of folic acid, vitamin B6 and B12 for the treatment of depressed or inadequate intracellular pyridoxal phosphate levels in a human or animal and Paul et al. teach a method of providing sustained energy and nutrition for anabolic physiological state in a human by administering to said human a nutritional composition containing carbohydrates, lipids, protein and magnesium in the form of amino acid chelate and other vitamins and nutrients, one skilled in the art would have a reasonable expectation for success in combining both references to accomplish a pharmaceutical composition for the treatment for serotonin- or melatonin-mediated disorders.

Claims 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Serfontein (U.S. Patent 5,631,271) of record.

Claims 29 and 30 are drawn to a pharmaceutical composition for treatment of serotonin- or melatonin-mediated disorders, containing more than 44 µg of folic acid, more than 0.8 µg of vitamin B12, more than 50 µg of vitamin B6, and further containing at least one group consisting of riboflavin, thiamin, niacin and zinc.

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Serfontein discloses a pharmaceutical composition in col. 10, lines 38-62, that is essentially a combination of vitamin B6, folate and vitamin B12. Serfontein also suggests in col. 12, lines 1-10, the daily dosages of ingredients in an infant food formula in the ranges of vitamin B6 (0.01-5 mg), riboflavin (0.01-5 mg), folate (.001-0.5 mg) and vitamin B12 (0.01-10 μ g). Serfontein differs from the applicant's invention that Serfontein does not provide an explicit example of a nutritional composition for the treatment of serotonin- or melatonin-mediated disorders which comprises thiamin, however Serfontein does provide motivation to use vitamin B6, riboflavin, folate, vitamin B12 in a pharmaceutical composition. Use of a known member of a class of materials in a process is not patentable if other members of the class were known to be useful for that purpose, even though results are better than expected.

Therefore, one of ordinary skill in the art would have found the applicants claimed pharmaceutical composition containing folic acid, vitamin B12, vitamin B6 and further containing at least one group consisting of riboflavin, thiamin, niacin and zinc, wherein folic acid is more than 44 μ g, vitamin B12 is more than 0.8 μ g and vitamin B6 is more than 50 μ g, to have been obvious at the time the invention was made having the above reference before him because Serfontein teaches a composition comprising vitamin B6, folate and vitamin B12, for treatment and prophylaxis of metabolic disturbances in infants.

Rejection Maintained

Rejection of claims 18,19,21-25,28-30 under 35 U.S.C. 103(a) is maintained. New claims 31-34 are also rejected under 35 U.S.C. 103(a) as being unpatentable over

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Serfontein (U.S. Patent 5,631,271) in view of Paul et al. (U.S. Patent 5,292,538), as already applied to claims 16-28. The amended claim 29 and new claims 31-34 claim a method of prevention of serotonin- or melatonin-mediated disorders. However, the applicant fails to provide sufficient guidance or support to enable the worker of ordinary skill in the art for preventing serotonin- or melatonin-mediated disorders by the administration of an effective amount of a combination of carbohydrates, fats, proteins, folic acid, vitamin B6 and B12 and at least one component selected from the group consisting of riboflavin, thiamin, niacin and zinc. Therefore, rejection of new claims 31-34 and amended claims 18-30 under 35 U.S.C. 112, first paragraph, is maintained. In the newly added claims 31-34, applicants claim a method for treating serotonin- or melatonin-mediated disorders with a composition comprising carbohydrates, fats, proteins, folic acid, vitamin B6 and B12 and at least one component selected from the groups consisting of riboflavin, thiamine, niacin and zinc. Since previous claims 16-28 include the same method for treating serotonin- or melatonin-mediated disorders, claims 31-34 are obvious within the prior art already set forth in the rejections of claims 16-28.

Response to Arguments

Applicant's arguments filed on July 15, 2003 traversing the rejection of claims 16-30 under 35 U.S.C 103(a), obvious over Serfonstein ('271) in view of Paul et al. ('538), have been fully considered but they are not persuasive.

Applicants argue that "Serfonstein is concerned with treating problems in the conversion of pyridoxine (the common vitamin B6 precursor) to pyridoxal (the active form of vitamin

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B6)” and “the amounts of the specific vitamins as described by Paul et al. are low, compared to the present invention”. Serfonstein (‘271) does not specifically disclose the treatment of melatonin- and serotonin-mediated disorders, however Serfonstein discloses the use of a composition containing vitamin B6, riboflavin, folate, vitamin B12 and protein, fat and carbohydrate, for treatment and prophylaxis of metabolic disturbances in infants (col. 31, Example 10). Serfonstein also disclose that an enzymatic disturbance or insufficiency can be due to chemical factors (internal or externally introduced (col. 15, lines 47-55). Paul et al. disclose the formulation containing minerals and nutrients that enhance the utilization of carbohydrates, proteins and lipids (see col. 6, lines 54-58). Applicant has not demonstrated any criticality or unexpected result, which stems from selection of specific vitamins lower in amounts than suggested by Paul et al.

2. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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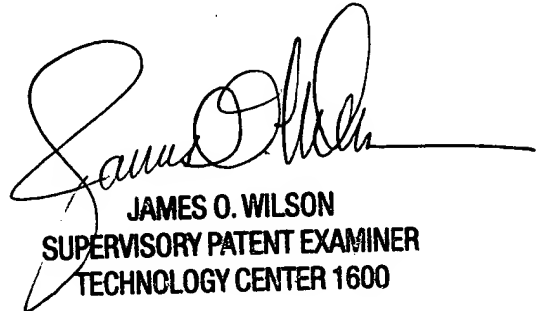
the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Devesh Khare whose telephone number is (703)605-1199. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at 703-308-4624. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Devesh Khare, Ph.D.,JD(3Y).
Art Unit 1623
October 10,2003



JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
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